REMARKS

I. Support for the Amendments

The present application is a 35 U.S.C. §371 national stage of PCT application PCT/JP00/05639, filed August 23, 2000, which claims priority of Japanese Application Serial Number 236597, filed August 24, 1999. Support for the amendment to the specification inserting the Cross-References to Related Applications can be found in the transmittal papers, in the published PCT application, and in the Declaration & Power of Attorney.

The amendments to page 7 of the specification (Brief Description of the Drawings) are simply a matter of form and are made in part to make the specification consistent with the amended Figure. Support for the amended paragraph can be found in the specification as filed.

Similarly, the amendment to page 72 is also a matter of form.

Claims 1 and 3-11 are presently in the application. Claims 1 and 3 have been amended, new claims 4-11 have been added, and non-elected claim 2 has been canceled without prejudice to its pursuit in an appropriate continuation or divisional application. Claims 1 and 3 are the independent claims.

Support for amended claims 1and 3 and for new claims 4-11 can be found in the original specification and claims. Additional support for amended claims 1 and 3 can be found, e.g., from page 3, line 14, to page 7, line 7; from page 7, line 19, to page 67, line 3; on page 7, lines 19-21; on page 10, lines 11-21; from page 17, line 31, to page 19, line 3; from page 19, line 27, to page 23, line 12; from page 24, line 1, to page 36, line 4; from page

36, line 5, to page 39, line 21; from page 40, line 1, to page 42, line 7; from page 46, line 14, to page 53, line 2; from page 56, line 17, to page 58, line 4; from page 58, line 26, to page 60, line 34; and in the Examples. Additional support for new claims 4-11 can be found, e.g., on pages 31, 34-35, and 71; and in the Examples.

The Abstract (pages 74-75) has been amended as requested by the Examiner. Support for the amended Abstract can be found in the specification as filed.

II. Status of the Claims

Claims 1-3 were originally in the application, with claims 1 and 3 being the independent claims. Claims 1-3 were subject to an Election/Restriction Requirement, and claims 1 and 3 (Group I) were elected with traverse.

Claims 1 and 3-9 are currently in the application. Claims 1 and 3 have been amended, and new claims 4-11 have been added. Non-elected claim 2 has been canceled without prejudice. Claims 1 and 3 are the independent claims. Claims 4-7 are dependent on claim 1, and claims 8-11 are dependent on claim 3.

III. The Priority Application

Applicants thank the Examiner for acknowledging the priority claim based on Japanese Application 236597/1999, filed in Japan on 24 August 1999. The Office Action states:

> It is noted, however, that applicant has not filed a certified copy of the 236597/1999 application as required by 35 U.S.C. 119(b). [P. 3; par. 5.]

Applicants wish to note on record that a certified copy of the Japanese priority application 236597/1999 was received in the International Bureau of WIPO on 13 October 2000, as shown on Form PCT/IB/304, a copy of which was filed in the U.S. Patent & Trademark Office on February 21, 2002, together with the application. The certified copy should have been communicated by the International Bureau directly to the U.S. Patent & Trademark Office. From the record, therefore, it does not appear that Applicants are required to make any further submissions.

IV. The Information Disclosure Statement

Applicants thank the Examiner for acknowledging the Information Disclosure Statement.

V. The Objection to the Drawing

The Examiner has objected to the drawing and requested correction. Applicants have amended the drawing in accordance with the Examiner's remarks. In addition, Applicants have amended the specification to be consistent with the amendments to the drawing.

VI. The Objections to the Specification

First, the Examiner has objected to the length and format of the Abstract. Applicants have provided an amended Abstract and respectfully request reconsideration thereof.

Second, the Examiner has noted that the claims should be the object of a sentence. Applicants have amended the first claim sheet (page 72) accordingly.

VII. The Rejection of Claims 1 and 3 under 35 U.S.C. §112, Second Paragraph is Traversed in Part and Accommodated in Part

The Examiner has rejected claims 1 and 3 under 35 U.S.C. §112, second paragraph (pp. 4-6).

The Patent Office alleges:

14. Claims 1 and 3 are indefinite for reciting the phrase "capable of expressing". Does this refer to a cell that actually expresses the receptor (naturally or as a result of genetic manipulation) all of the time, part of the time, or only in the proper conditions, or does it refer to any cell that could potentially express the receptor protein if were transfected with the appropriate cDNA.

15. Claims 1 and 3 are further indefinite because the metes and bounds of the limitation "a common structure" cannot be clearly determined. It is unclear how much the structure of the candidate compound can deviate from a referenced structure and still have "a common structure".

16. Claims 1 and 3 are further rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Part (iii) of each claim, "by considering a common structure", does not set forth any steps involved in the method/process, therefore it is unclear what method/process is encompassed by the claim.

17. Claims 1 and 3 are further rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Part (iiii) of each claim, measuring amount of specific binding between said orphan receptor protein and test compound, does not set forth any steps involved in the method/process, therefore it is unclear what method/process is encompassed by the claim. Furthermore, the same holds true for parts (b), (c), (d), (e), and (f) of the claim.

18. Claims 1 and 3 are further indefinite for reciting the phrase "measuring a cell stimulating activity to be measured" in parts (i) and (iii) of claim 1 and part (i) of claim 3. It is unclear how one would compare an activity that has not been measured yet, i.e, "to be measured".

19. Claim 1 is further indefinite because the two parts of claim 1, part (iii), do not relate to each other.

20. Claim 1 is further indefinite because part (iii) of the claim does not clearly relate back to the preamble. It is not clear how measuring the amount of

specific binding in part (iii) of the claim identifies a compound that promotes or inhibits a function of an orphan receptor protein. [Pp. 5-6; pars. 14-20.]

Applicants disagree, but respectfully submit that the amendments to claims 1 and 3 address these points.

With respect to paragraph 14, the term "express" and similar terms have been substituted for "capable of expressing" in accordance with the Examiner's remarks.

With respect to paragraph 15, Applicants respectfully refer the Examiner to the discussion, e.g., at pages 34-35 of the specification. Applicants submit that "a common structure" refers to a homology and/or a similarity in a steric structure between or among compounds. For example, when the agonist is a peptide, one example provided of a common structure is "R-X-NH_3 structure at C-terminus" (see, e.g., p. 35). When the agonist is a non-peptide, one example provided of a common structure is a "cycloalkyl" (see, e.g., p. 35).

Moreover, those skilled in the art would be able to recognize an appropriate extent of deviation from a common structure from a referenced structure based on the description at pages 34-35 and related descriptions in the present specification. In the present screening method, a candidate compound is firstly selected based on a common structure, and then the selected candidate compound is further screened based on an amount of specific binding. If the common structure is deviated from a referenced structure to a great extent, then the next screening step based on the amount of the specific binding would become laborious, and if the common structure is deviated from a reference structure to a small extent, then the next screening step based on the amount of the specific binding would be relatively easy, because the structure of a compound is normally correlated to its activity. Therefore, those skilled in the art would be able to know or predict which structures would have a reasonable

expectation of success and therefore determine an appropriate extent of the deviation of a common structure from a referenced structure depending on their purpose and/or conditions.

With respect to paragraphs 16-17, Applicants have amended the claims to recite a step of extracting a common structure among the compounds having the agonist activity in order to identify ligand candidate compounds. The remarks with respect to paragraph 15 also apply here. In addition, claim 1 is further amended to recite specifically how a compound which promotes or inhibits a function of an orphan receptor protein is screened via the claimed process by measuring the amount of specific binding between the orphan receptor protein and test compound (b). Claim 3 is also further amended to specifically recite how a ligand or its subtype of an orphan receptor protein is selected by measuring amount of specific binding between said orphan receptor protein and the ligand candidate compound. Therefore, amended claims 1 and claim 3 contain essential steps and are thus complete.

With respect to paragraph 18, Applicants have deleted the phrase "to be measured."

With respect to paragraphs 19-20, claim 1 has been amended such that the two parts of claim 1, part (iii) relate to each other. In addition, claim 1 has been amended to further describe how measuring the amount of specific binding in part (iii) of the claim identifies a compound that promotes or inhibits a function of an orphan receptor protein.

Applicants respectfully submit that the present amendments to claims 1 and 3 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, second paragraph, thereby placing these claims in condition for allowance.

VIII. The Rejection of Claims 1 and 3 Under 35 U.S.C. §102(b) with Respect to Aiyar Is Traversed, but Accommodated

The Examiner has rejected claims 1 and 3 under 35 U.S.C. §102(b) as being anticipated by Aiyar et al. (J. Biol. Chem. 271(19): 11325-11329 (1996); "Aiyar") (pp. 6-7). Applicants respectfully disagree.

The Patent Office alleges:

> Aiyar et al. teach a screening method to identify a test compound (CGRP) which binds to membrane fractions obtained from cells transformed with an orphan receptor as well as membrane fractions of untransfected cells as a control (See Experimental Procedures: Binding Assays, page 11326; Figure 3, page 11327). Aiyar et al also teach a functional assay method to identify a test compound that stimulates activity in cells that are transformed with an orphan receptor as well as untransfected cells as a control via measuring cyclic AMP (See Experimental Procedures: Functional Assays, page 11326; Figure 4, page 11328). In both screening methods, Aiyar et al. additionally teach the screening of molecules that are analogs of CGRP (See Figures 3 and 4). Thus, Aiyar et al. teach all the limitations of claims 1 and 3. [Pp. 6-7; par. 22.]

Applicants respectfully disagree and traverse the anticipation rejection. Aiyar describes a cloning of a receptor of CGRP which is identified among ESTs based on its similarity in amino acid sequence to calcitonin receptors. Aiyar uses CGRP receptor agonists or antagonists which were obtained by previous pharmacological studies that were performed prior to the cloning of the CGRP receptor. The description relating to similarity in **Aiyar is only directed to the primary sequence of the receptor**, and there is **no description** regarding **extraction and/or determination** of a **common structure of agonists or antagonists** used therein.

Thus, there is clear distinction between the present invention and the cited reference in that claimed invention is based on **the inventive concept of extraction and/or determination of a common structure of agonists or antagonists** and contain an actual

step therefor, while the cited references lack the concept and the actual step therefor. There is no suggestion or teaching regarding extraction and/or determination of a common structure of agonists or antagonists in the cited reference.

Applicants respectfully submit that the present claims 1 and 3 fulfill the requirements of 35 U.S.C. §102(b) and request the Examiner's reconsideration of this claim accordingly.

IX. The Rejection of Claims 1 and 3 Under 35 U.S.C. §102(b) with Respect to Zhou Is Traversed

The Examiner has rejected claims 1 and 3 under 35 U.S.C. §102(b) as being anticipated by Zhou et al. (Proc. Natl. Acad. Sci. USA, 89:7432-7436 (1992); "Zhou"). Applicants respectfully disagree.

The Patent Office alleges:

> Zhou et al. teach a screening method to identify a test compound which binds to membrane fractions obtained from cells transformed with an orphan receptor as well as membrane fractions of untransfected cells as a control (See Results, page 7433 ¶3; Figure 3, page 7435). Aiyar et al also teach a functional assay method to identify a test compound that stimulates activity in cells that are transformed with an orphan receptor as well as untransfected cells as a control via measuring cyclic AMP (See Results, page 7433-7435; Figure 4A, page 7435). In both screening methods, Zhou et al. additionally teach the screening of molecules that are analogous compounds (See Figures 3 and 4, page 7435). Thus, Zhou et al. teach all the limitations of claims 1 and 3. [P. 7, par. 23.]

Applicants respectfully disagree and traverse the anticipation rejection. Zhou describes a cloning of a novel adenosine receptor subtype which is identified among cDNA fragments obtained using a denatured primer based on its similarity in amino acid sequence to known adenosine receptors. Zhou used adenosine receptor agonists or antagonists which had been obtained by previous pharmacological studies that were performed to compare their properties with those of known adenosine receptors. Description relating to structural

similarity in **Zhou is only directed to the primary sequence of the receptor**, and there is **no description** regarding **extraction and/or determination** of a **common structure of agonists or antagonists** used therein.

Thus, there is clear distinction between the present invention and the cited reference in that claimed invention is based on the inventive concept of extraction and/or determination of a common structure of agonists or antagonists and contain an actual step therefor, while the cited references lack the concept and the actual step therefor. There is no suggestion or teaching regarding extraction and/or determination of a common structure of agonists or antagonists in the cited reference.

Applicants respectfully submit that the present claims 1 and 3 fulfill the requirements of 35 U.S.C. §102(b) and request the Examiner's reconsideration of these claims accordingly.

X. Request for Filing Receipt

Applicants have not yet received an Official Filing Receipt. Applicants have filed Requests for an Official Filing Receipt on September 21, 2004, and on February 8, 2005, but have not received a response. Applicants respectfully request any assistance the Examiner could provide in obtaining an Official Filing Receipt.

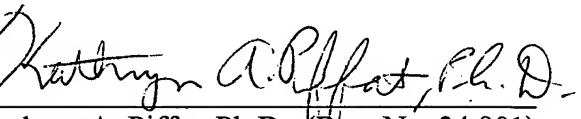
XI. Conclusion

It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants believe that no extension of time is required for the Amendment and accompanying materials. If an extension of time is required, Applicants hereby request the Examiner to consider this a conditional petition for an extension of time. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,



Date: April 27, 2005

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PATENT COOPERATION TREATY

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NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/year) 03 November 2000 (03.11.00)	
Applicant's or agent's file reference 2639WO0P	**IMPORTANT NOTIFICATION**
International application No. PCT/JP00/05639	International filing date (day/month/year) 23 August 2000 (23.08.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 24 August 1999 (24.08.99)
Applicant TAKEDA CHEMICAL INDUSTRIES, LTD. et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
24 Augu 1999 (24.08.99)	11/236597	JP	13 Octo 2000 (13.10.00)

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